

# IL-33 may augment the effect of rhinovirus HRV16 on the inflammatory activity of human lung vascular endothelium – possible implication for rhinoviral asthma exacerbations

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## Introduction

Human rhinovirus (HRV) may cause severe asthma exacerbations, which is accompanied by increased airway IL-33 concentrations.

## Aim

To analyze the effect of IL-33 on the HRV-induced anti-viral and inflammatory response by the lung vascular endothelium.

## Material and methods

Human pulmonary microvascular endothelial cells (HMVEC-L) were exposed to HRV-16 (MOI3) alone or upon the pre-stimulation with IL-33 (10 ng/ml) and cultured for 72 h. HRV-16 copy number in HMVEC-L, cytokine, chemokine and growth factors mRNA expression were assessed in real-time PCR. Protein concentrations were assessed in BioPlex, while ICAM-1 expression in the flow cytometry and confocal microscope.

## Results

HRV16 strongly increased the release of inflammatory cytokines, including IL-1 $\beta$ , IL-6, TNF- $\alpha$ , RANTES and IP-10, chemokines: MIP-1 $\alpha$ , MIP-1 $\beta$ , IL-8 and eotaxin as well as growth factors: G-CSF, GM-CSF, FGF and VEGF ( $p < 0.05$ ). Furthermore, HRV16 enhanced both mRNA expression and protein release of type I interferons (IFN- $\beta$  and  $\lambda$ ,  $p < 0.05$ ) as well as immunomodulatory cytokines: IL-12, IFN- $\gamma$ , IL-4, IL-5, IL-13, IL-17 ( $p < 0.05$ ), but not IL-10. IL-33 increased the capture of HRV16 particles associated with the up-regulation of ICAM-1 surface expression ( $p < 0.05$ ). IL-33 enhanced HRV16-

induced release of IL-1 $\beta$ , IL-6 ( $p < 0.05$ ), but not RANTES, IP-10, TNF- $\alpha$  production. IL-33 enhanced HRV16-induced release most of growth factors and chemokines ( $p < 0.05$ ), but not MIP-1 $\beta$  and MCP-1. Finally, IL-33 enhanced HRV16-induced release IL-12 (not IFN- $\gamma$ ), IL-4, IL-5, IL-13, IL-17, and IL-10 ( $p < 0.05$ ).

## Conclusions

IL-33 may augment the effect of rhinovirus on inflammatory, but not antiviral, activity of the lung vascular endothelium, and thus facilitate heavy exacerbations of asthma. National Science Center 2017/25/B/ NZ5/01575.